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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/117,447 12/02/98 LUBITZ

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HM12/0716

EXAMINER

MINNIFIELD, N

ART UNIT

PAPER NUMBER

1645

DATE MAILED:

07/16/01

15

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks**BEST AVAILABLE**

Office Action Summary

Application No.

09/117,447

Applicant(s)

LUBITZ ET AL

Examiner

N. M. Minnifield

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1645



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on Apr 23, 2001

2a) This action is FINAL. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle* 1835 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) Claim(s) 1-17, 19-24, 26, 28-30, 32-34, and 37-65 is/are pending in the applica

4a) Of the above, claim(s) 21-24, 26, 28-30, 32-34, 37-45, and 48-57 is/are withdrawn from considera

5) Claim(s) _____ is/are allowed.

6) Claim(s) 1-17, 19, 20, 46, 47, and 58-65 is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claims 1-17, 19-24, 26, 28-30, 32-34, and 37-65 are subject to restriction and/or election requirem

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are objected to by the Examiner.

11) The proposed drawing correction filed on _____ is: a) approved b) disapproved.

12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) All b) Some* c) None of:

1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) Notice of References Cited (PTO-892)

18) Interview Summary (PTO-413) Paper No(s). _____

16) Notice of Draftsperson's Patent Drawing Review (PTO-948)

19) Notice of Informal Patent Application (PTO-152)

17) Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____

20) Other: _____

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DETAILED ACTION

1. Applicants' amendment filed April 23, 2001 is acknowledged and has been entered. Claims 1-17, 19, 20, 46 and 47 have been amended. New claims 58-65 have been added. Applicants have added 8 new claims; however these claims were incorrectly numbered and as per Rule 1.126 the new claims 48-55, as numbered by Applicants, have been renumbered 58-65. Claims 1-17, 19, 20, 46, 47 and 58-65 are now pending in the present application. All rejections have been withdrawn in view of Applicants' amendment with the exception of those discussed below.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
3. This application contains claims 21-24, 26, 28-30, 32-34, 37-45, and 48-57 are drawn to an invention/species nonelected with traverse in Paper No. 8 and 11. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 C~~A~~R 1.144) See ^{MPEP} M.E.P.. § 821.01.
4. Claims 5-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 5-12 recite the limitation

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"insertions". There is insufficient antecedent basis for this limitation in claim 4; claim 4 recites "insertion".

5. Applicants deposit information and viability statement have been received and reviewed. The objection and rejection under 35 U.S.C. § 112, first paragraph has been withdrawn.

6. Claims 1, 3, 15-17, 19, 20, 46 and 47, and now 58-63 are rejected under 35 U.S.C. 102(b) as being anticipated by Kuen et al (*Gene*, 1994).

The claims are directed to a nucleic acid sequence, cells, vectors, and a process of producing S-layer proteins.

Kuen et al disclose that the S-layer protein was cloned and expressed in a prokaryotic cell system and discloses the nucleic acid sequence of the S-layer protein (abstract; p. 116, col. 1). The prior art discloses cells for transformation and a vector (p. 116, Experimental and Discussion). Kuen et al disclose the nucleotide sequence including signal sequence of the *sbs* gene which encodes the S-layer protein (p. 117, col. 2; figure 2; table 1; p. 119, col. 2). Kuen et al anticipates the claimed invention.

The rejection is maintained for the reason of record. Applicant's arguments filed April 23, 2001 have been fully considered but they are not persuasive. It is noted that Applicants state that the authors of Kuen et al are

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inventors. It is noted that this a 102(b) rejection, the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Applicants have asserted that Kuen et al does not describe the expression of a complete sbsA gene in *E. coli*; however this language is not in the claims. Applicants also state that the prior art negative results are due to the full sbsA gene being either unstable or toxic when expressed in *E. coli* and that Applicants have overcome the problem by applying PCR cloning and sequencing strategies to isolate and determine sequence of missing 5' fragment of the Bs sbsA gene. However, it is noted that Kuen et al disclose: "In the present study we report the complete nt sequence of the sbsA gene of Bs PV72. Instabilities due to rearrangements within the 5' end of the sbsA gene during cloning were overcome by direct synthesis using PCR." (p. 119, right column).

The prior art appears to disclose the claimed invention. Since the Office does not have the facilities for examining and comparing applicants' products and methods with the products and methods of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and method of the prior art (i.e., that the product and method of the prior art does not possess the same material structural and functional characteristics of the

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claimed products and methods). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

7. Claims 1-17, 19, 20, 46 and 47, and now 58-65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kuen et al (Gene, 1994) taken with Deblaere et al (WO9519371).

The claims are directed to a nucleic acid sequence, cells, vectors, and processes of producing S-layer proteins or S-layer proteins with an insertion (enzymes, antigens, immunogens, etc).

Kuen et al teach that the S-layer protein was cloned and expressed in a prokaryotic cell system and teach the nucleic acid sequence of the S-layer protein (abstract; p. 116, col. 1). The prior art teaches cells for transformation and a vector (p. 116, Experimental and Discussion). Kuen et al teach the nucleotide sequence including signal sequence of the *sbs* gene which encodes the S-layer protein (p. 117, col. 2; figure 2; table 1; p. 119, col. 2). Kuen et al teach the claimed invention except for the concept of insertion of heterologous proteins/polypeptides.

However, Deblaere et al teach a host cell which is provided with an S-layer comprising a fusion polypeptide consisting essentially of the S-layer protein and a heterologous polypeptide (abstract; p. 6; claims). Deblaere et al teach that the gene for the S-layer protein includes strong promoter sequences, signal peptide

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coding sequences as well as a transcription termination sequence (p. 2). The prior art teaches recombinant DNA molecules that includes a SLP system capable of expressing and presenting a fusion polypeptide in a wide variety of bacteria (p. 5). Deblaere et al teach that the insertion or heterologous protein can be a physiologically active polypeptide such as an enzyme, a polypeptide drug or a cytokine (interferon), foreign epitope or polypeptide immunogen, etc (p. 9). The immunogen can be an antigen of a pathogen such as a virus, bacterium, fungus, yeast or parasite (pp. 9-10). Further, the prior art teaches expression vectors and suitable host cells as well as methods of producing the proteins (p. 10-12). It would have been obvious to a person of ordinary skill in the art at the time the invention was made to use the methods/processes as taught by both Kuen et al and Deblaere et al with the reasonable expectation of success of obtaining a process to produce pure S-layer protein, a recombinant S-layer protein or a fusion protein comprising the S-layer protein having an insertion of a heterologous polypeptide as presently claimed. Kuen et al sets forth nucleotide sequence of the S-layer protein while both references provide the process methods, cells, and vectors. Deblaere et al provides the motivation and suggestion to insert foreign or heterologous protein (DNA) into the DNA of the S-layer for the purpose of making fusion proteins that are expressed. It is noted that the prior art does not specifically teach the insertion at the specific positions that are set forth in claim 16; however it would have been obvious to a person of ordinary skill in the art at

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the time the invention was made to insert the foreign DNA at any cleavage site that would still allow for the assembly of the S-layer protein. The claimed invention is *prima facie* obvious in view of the teachings of Kuen et al taken with Deblaere et al, absent any convincing evidence to the contrary.

The rejection is maintained for the reasons of record. Applicant's arguments filed April 23, 2001 have been fully considered but they are not persuasive. Applicants have asserted that they are claiming a nonobvious expression system for a recombinant SLP and a fusion SLP polypeptide, using gram-negative bacteria, preferably *E. coli* as the host cell. Applicants also asserted that the S-layer protein of *B. sphaericus* shares no homology with the sbsA S-layer protein of the present invention. However, the claims do not recite the specific source of the S layer protein and the combination of teachings from Keun et al taken with Deblaere et al teach a fusion protein or heterologous protein (S-layer protein and another protein). Applicants assert that Deblaere et al does not teach expressing the SLP in a gram negative strain of bacteria and the unexpected advantage is that capacity of S-layer protein to form a correctly folded S-layer structure is not lost despite insertions being made to nucleic acid. The prior art (Deblaere et al teach that the host cell can be gram positive or gram negative. Further, obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references

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themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

8. No claims are allowed.

9. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be

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calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to N. M. Minnifield whose telephone number is (703) 305-3394. The examiner can normally be reached on Monday-Thursday from 7:00 AM-4:30 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette R. F. Smith, can be reached on (703) 308-3909. The fax phone number for Technology Center 1600 is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.



N. M. Minnifield
PRIMARY EXAMINER

N. M. Minnifield

July 10, 2001